

IN THE CLAIMS

The following list of claims replaces all previous claims in this application.

1. (currently amended) A biocompatible hydrogel-forming tissue-bonding adhesive composition, the composition comprising:

~~one or more at least one block copolymer polyols polyol~~ wherein each hydroxyl of said block copolymer polyols polyol is terminated with a low molecular weight polyisocyanate, said terminated block copolymer polyols polyol being liquid and water-soluble;

and wherein said block copolymer polyols polyol ~~[[have]] has a~~ functionality averaging N at least 1.5, and wherein at least 1% ~~— (N-1)%~~ of said composition by weight, but not more than 5% of said composition by weight, comprises a low molecular weight free polyisocyanate, which may be the same as the polyisocyanate terminating the block copolymer polyols;

and wherein on average in the solution composition, 10% to 30% of the monomers of said block copolymer polyol polyols are derived from propylene oxide monomers, and the rest of the monomers are ethylene oxide derived monomers;

characterized in that after polymerization, upon exposure to tissue or water, the adhesive composition forms a hydrogel comprising, after equilibration with water or aqueous fluids, greater than 50% water by volume; and

wherein the composition polymerizes in situ upon exposure to water and application to tissue, without requiring the addition of a catalyst.
2. (currently amended) The biocompatible composition as recited in claim 1 wherein N the copolymer polyol polyols have has a functionality averaging 3. is 1.5—8.

3. (currently amended) The biocompatible composition as recited in claim 1 wherein at least one polyol of said polyols is a branched polypropylene oxide/polyethylene oxide block copolymer.
4. (cancelled)
5. (currently amended) The biocompatible composition as recited in claim 3 wherein said composition further comprises a polypropylene oxide/polyethylene oxide copolymer which contains no more than 10% propylene oxide units.
6. (previously presented) The biocompatible composition as recited in claim 1 wherein said polyisocyanate is selected from toluene diisocyanate and isophorone diisocyanate.
7. (previously presented) The biocompatible composition as recited in claim 1 wherein said polyisocyanate comprises 2,6-toluene diisocyanate.
8. (previously presented) The biocompatible composition as recited in claim 1 wherein said polyisocyanate comprises isophorone diisocyanate.
9. (previously presented) The biocompatible composition as recited in claim 1 wherein said polyisocyanate comprises an 80:20 mixture of 2,4- toluene diisocyanate and 2,6-toluene diisocyanate and about 3% of the composition is free polyisocyanate.
10. (previously presented) The biocompatible composition as recited in claim 1 wherein said polyisocyanate comprises isophorone diisocyanate and about 1.5% of said composition is free polyisocyanate.
11. (original) The biocompatible composition as recited in claim 1, wherein said composition is comprised of two polyisocyanates and wherein one of said polyisocyanates comprises a free isocyanate B as an aromatic polyisocyanate and the other of said polyisocyanates comprises an aliphatic isocyanate A which is used to endcap said copolymer.
12. (original) The biocompatible composition as recited in claim 11 wherein the free isocyanate B converts to an amine faster than the isocyanate A.

13. (original) The biocompatible composition as recited in claim 11 wherein said free isocyanate B is more reactive with nitrogenous substances than said isocyanate A.
14. (original) The biocompatible composition as recited in claim 11 wherein said free isocyanate B is of lower viscosity than said isocyanate A.
15. (cancelled)
16. (cancelled)
17. (currently amended) A biocompatible hydrogel-forming adhesive composition comprising at least two branched block polyols wherein at least one of said polyols is a branched polypropylene oxide/polyethylene oxide copolymer, and wherein at least one of said branched polyols consists of a copolymer of less than 10% polypropylene oxide and at least one of said branched polyols comprises a copolymer consisting of between about 10 and 30% polypropylene oxide monomers, the remainder of each of said branched polyols consisting of ethylene oxide monomers, said copolymers of functionality in the range of 1.5-8, said copolymers being terminated with at least one polyisocyanate, said terminated copolymers forming a solution, and wherein at least 1% of said solution but less than not more than 5% of said solution [[,]] comprises free polyisocyanate;
characterized in that after polymerization, upon exposure to tissue or water, the adhesive forms a hydrogel comprising greater than 50% water by volume; and
wherein the composition is suitable for use as a biocompatible tissue-bonding adhesive composition.
18. (previously presented) The biocompatible composition as recited in claim 17 wherein one of said polyol copolymers comprises 5% polypropylene oxide and the other of said polyol copolymers comprises 25% polypropylene oxide.
19. (previously presented) The biocompatible composition as recited in claim 20 wherein said copolymer having a lesser functionality comprises at least 25% of the number of polymer molecules of the total copolymer component.

20. (previously presented) The biocompatible composition as recited in claim 17 wherein one of said copolymers has a lesser functionality than one or more of the other of said copolymers.
21. (original) The biocompatible composition as recited in claim 20 wherein one of said copolymers has functionality 2 and the other of said copolymers has functionality 3.
22. (previously presented) The biocompatible composition as recited in claim 20 wherein said copolymer of lesser functionality is less than 25% of the number of polymer molecules of the total copolymer component.
23. (previously presented) The biocompatible composition as recited in claim 22, wherein one polyol is terminated with a polyisocyanate having a first reaction rate with water R1 and another polyol is terminated with a polyisocyanate having a second reaction rate with water R2, where R1 is a faster rate than R2, both of said terminated polyols having an average functionality of 1.5-8, said terminated polyols being in a solution, with at least 1% of said solution comprising free polyisocyanate of reactivity R1.
24. (previously presented) The biocompatible composition as recited in claim 23 wherein one of said polyols is terminated with an aromatic polyisocyanate and another of said polyols is terminated with an aliphatic polyisocyanate, both of said polyols having an average functionality of 1.5-8, said terminated polymers being in solution, wherein at least 1% of said solution comprises free polyisocyanate.
25. (original) The biocompatible composition as recited in claim 24 wherein said free polyisocyanate is aromatic.
26. (previously presented) The biocompatible composition as recited in claim 25, wherein said free polyisocyanate comprises toluene diisocyanate.
27. (previously presented) The biocompatible composition as recited in claim 25, wherein said free polyisocyanate consists of one or more isomers of 2,6-toluene diisocyanate.
28. (previously presented) The biocompatible composition as recited in claim 23, wherein said composition eliminates any aromatic amines induced by reaction

of water or proteins with aromatic isocyanates during polymerization, said elimination occurring by reaction of such aromatic amines with less-reactive aliphatic isocyanates capping polyols, where the number of groups of said less reactive isocyanate capped polyol is present in essentially stoichiometric amounts with respect to said the number of groups of said aromatic isocyanates.

29. (previously presented) The biocompatible composition as recited in claim 28, wherein said less reactive isocyanate capping said polyol comprises isophorone diisocyanate.
30. (previously presented) The biocompatible composition as recited in claim 29, wherein said polyol is a block polyol containing 75% polyethylene oxide and 25% polypropylene oxide.

31 - 39 (cancelled)

40. (currently amended) A biocompatible hydrogel-forming tissue-bonding adhesive composition comprising:

at least one block ethylene oxide-propylene oxide copolymer polyol, said composition comprising 10% to 30% propylene oxide monomers on average, of average functionality $[[N]]$ 1.5 - 8, said polyol being terminated with at least one polyisocyanate, with at least ~~(N-1)%~~ 1% and less than 5% of said composition comprising free polyisocyanate,

characterized in that after polymerization, upon exposure to tissue or water, the adhesive forms a hydrogel comprising greater than 50% water by volume; and

wherein the composition is suitable for use as a biocompatible tissue-bonding adhesive composition.

41. (currently amended) The biocompatible composition as recited in claim 40 wherein the average functionality is 3. N is in the range 1.5 - 8.

42. (currently amended) The biocompatible composition as recited in claim 40 wherein said polyol comprises at least one branched ~~polypropylene/poly-ethylene propylene oxide/ethylene oxide~~ copolymer.

43. (cancelled)

44. (currently amended) The biocompatible adhesive of claim 40 wherein the adhesive is a one-part adhesive consisting essentially of at least one NCO-terminated branched polymer, derived from at least one polymeric polyisocyanate, and at least 1% unreacted low molecular weight ("free") polyisocyanate, wherein the adhesive is characterized in having a reactivity such that

- 1) free polyisocyanate bonds to tissue,
- 2) said free polyisocyanate converts to a polyamine and links said NCO-terminated branched polymer to said tissue bonded polyisocyanate; and
- 3) said free polyisocyanate converts to polyamine and links said branched polymer to other ~~said same~~ polymers.

45. (currently amended) The biocompatible adhesive of claim 40 wherein the adhesive is a one-part adhesive consisting essentially of two NCO-terminated branched ~~polypropylene oxide/polyethylene/poly-ethylene~~ oxide copolymers, wherein copolymer A is at most 10% polypropylene oxide and copolymer B is between about 10% and 30% polypropylene oxide, derived from a polymeric polyisocyanate and at least 1% and less than about 5% unreacted low molecular weight ("free") polyisocyanate,

wherein the adhesive is characterized in having a reactivity such that

- 1) free polyisocyanate bonds to tissue,
- 2) said free polyisocyanate converts to a polyamine and links both A and B type polypropylene/polyethylene oxide copolymers to said tissue bonded polyisocyanate,
- 3) said free polyisocyanate converts to polyamine and links said branched polypropylene/polyethylene oxide copolymers to other said polymers, and later,

4) polymerized copolymer A swells within the formed polymer matrix and causes degradation of the formed matrix.

46. (currently amended) The biocompatible adhesive of claim 40, wherein the adhesive is a one-part adhesive consisting essentially of two NCO-terminated branched polypropylene oxide/polyethylene oxide copolymers, wherein copolymer A is at most 10% polypropylene oxide and copolymer B is between 10% and 30% polypropylene oxide, and at least 1% but less than 5% unreacted low molecular weight ("free") polyisocyanate,

wherein the adhesive is characterized in having a reactivity such that

- 1) free polyisocyanate bonds to tissue;
- 2) said free polyisocyanate converts to a polyamine and links copolymer B preferentially to said tissue bonded polyisocyanate;
- 3) said free polyisocyanate converts to polyamine and links said branched polypropylene/polyethylene oxide copolymers to other said same polymers;
- 4) polymerized copolymer A swells within the formed polymer matrix and causes degradation of the formed matrix; and
- 5) polymerized copolymer B does not swell at the tissue/matrix interface and does not cause tissue bond degradation.

47. (previously presented) The biocompatible composition as recited in claim 40, wherein one polyol is terminated with a polyisocyanate having a first reaction rate with water R1 and another polyol is terminated with a polyisocyanate having a second reaction rate with water R2, where R1>R2, both of said terminated polyols having an average functionality of 1.5-8, said terminated polyols being in solution and with at least 1% of said solution comprising free polyisocyanate of reactivity R1.

48. (currently amended) The biocompatible composition as recited in claim 47 wherein one of said polyols is terminated with an aromatic polyisocyanate and another of said polyols is terminated with an aliphatic polyisocyanate, both of said polyols of

functionality 1.5-8, and said terminated polymers form [[in]] a liquid solution with at least 1% of said solution liquid comprising free polyisocyanate.

49. (previously presented) The composition of claim 40 wherein the polyols are capped by the isocyanates without the use of a catalyst.

50. (previously presented) The composition of claim 17 wherein the polyols are capped by the isocyanates without the use of a catalyst.

51. (currently amended) A composition bonding to tissue, comprising:

a liquid reactive component, comprising one or more polyol-terminated block polymers, each such polymer being entirely reacted with a low molecular weight organic polyisocyanate, said polymers having an average functionality of [[N]] 3, each said reacted polymer being a solvent for at least [[(N-1)%]] 1% but no more less than 5% by weight of a free low molecular weight organic polyisocyanate, which may be the same as the low molecular weight organic isocyanate reacted with said polymer;

wherein said liquid reactive component consists essentially of ethylene oxide and propylene oxide subunits and contains on average 10% to 30% propylene oxide; and

an activating component, consisting essentially of water, optionally containing medically compatible water soluble or miscible materials, which is mixed with the liquid reactive component at the time of application to tissue;

further characterized in that the mixture of reactive component and activating component creates a polymerizing mixture which adheres to any tissue it contacts during the polymerization.

52. (currently amended) A one-part biocompatible biodegradable hydrogel-forming tissue adhesive prepolymer composition, comprising:

a block polyol having a tri-functional structure containing ethylene oxide and 10% to 30% propylene oxide wherein each hydroxyl group of said polyol is terminated with a low molecular weight polyisocyanate without the use of a catalyst, the isocyanate

group to hydroxyl group ration ratio being in the range of 1.5 to 3.0, the terminated polyol being liquid and water-soluble;

wherein the prepolymer composition contains at least 1% and less than 5% free polyisocyanate and polymerizes to form a hydrogel upon application of the prepolymer to tissue resulting in exposure to water.